

**WHAT IS CLAIMED IS:**

1                   1.       A composition comprising a biologically active compound and a  
2 transport moiety, wherein the transport moiety comprises a structure selected from the group  
3 consisting of  $(\text{YZY})_n\text{Z}$ ,  $(\text{ZY})_n\text{Z}$ ,  $(\text{ZYY})_n\text{Z}$  and  $(\text{ZYYY})_n\text{Z}$ , wherein each Z is L-arginine or D-  
4 arginine, and each Y is independently an amino acid that does not comprise an amidino or  
5 guanidino moiety, and wherein n is an integer of from 2 to 10.

1                   2.       The composition according to claim 1, wherein each Y is  
2 independently selected from the group consisting of alanine, cysteine, aspartic acid, glutamic  
3 acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine,  
4 proline, glutamine, serine, threonine, valine, tryptophan, hydroxyproline, tyrosine,  $\gamma$ -amino  
5 butyric acid,  $\beta$ -alanine, sarcosine and  $\epsilon$ -amino caproic acid.

1                   3.       The composition according to claim 1, wherein the transport moiety  
2 comprises the structure  $(\text{YZY})_n\text{Z}$ , and wherein n is an integer ranging from 2 to 5.

1                   4.       The composition according to claim 1, wherein the transport moiety  
2 comprises the structure  $(\text{ZY})_n\text{Z}$ , and wherein n is an integer ranging from 4 to 10.

1                   5.       The composition according to claim 1, wherein the transport moiety  
2 comprises the structure  $(\text{ZYY})_n\text{Z}$ , and wherein n is an integer ranging from 4 to 10.

1                   6.       The composition according to claim 1, wherein the transport moiety  
2 comprises the structure  $(\text{ZYYY})_n\text{Z}$ , and wherein n is an integer ranging from 4 to 10.

1                   7.       The composition according to claim 1, wherein the transport moiety is  
2 attached to the biologically active compound by a linking moiety to form a conjugate.

1                   8.       The composition according to claim 1, wherein Y is a gene-encoded  
2 amino acid.

1                   9.       The composition according to claim 1, wherein Y is an amino acid  
2 other than a gene-encoded amino acid.

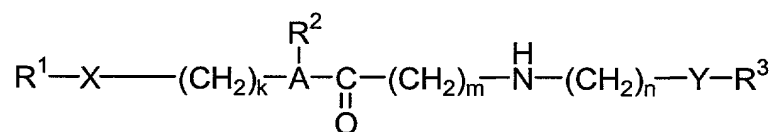
1                   10.      The composition according to claim 3, wherein each Y is  
2 independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine  
3 and  $\epsilon$ -amino caproic acid, and n is 3 or 4.

11. The composition according to claim 4, wherein each Y is independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine and  $\epsilon$ -amino caproic acid, and n is 6, 7 or 8.

12. The composition according to claim 5, wherein each Y is independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine and  $\epsilon$ -amino caproic acid, and n is 6, 7 or 8.

13. The composition according to claim 6, wherein each Y is independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine and  $\epsilon$ -amino caproic acid, and n is 6, 7 or 8.

14. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

$R^1$  is the biologically active compound ;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $R^1$  and  $R^3$ ;

Y is a linkage between a functional group on the transport moiety and a functional group on the linker between  $R^1$  and  $R^3$ ;

A is N or CH;

$R^2$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

$R^3$  is a transport moiety;

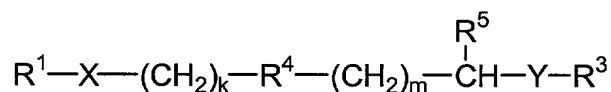
k and m are independently either 1 or 2; and

n is an integer of from 1 to 10.

15. The composition according to claim 14, wherein each of X and Y is independently selected from the group consisting of  $-C(O)O-$ ,  $-C(O)NH-$ ,  $-OC(O)NH-$ ,  $-S-S-$ ,  $-C(S)O-$ ,  $-C(S)NH-$ ,  $-NHC(O)NH-$ ,  $-SO_2NH-$ ,  $-SONH-$ , phosphate, phosphonate and phosphinate.

16. The composition according to claim 14, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

17. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R<sup>1</sup> is the biologically active compound ;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

R<sup>3</sup> is a transport moiety;

R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

R<sup>5</sup> is OH, SH or NHR<sup>6</sup>;

R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

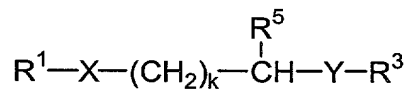
R<sup>7</sup> and R<sup>8</sup> are independently hydrogen, alkyl or arylalkyl; and

k and m are independently either 1 or 2.

18. The composition according to claim 17, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate and phosphinate.

19. The composition according to claim 17, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

20. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R<sup>1</sup> is the biologically active compound;

X is a linkage between a functional group on the biologically active compound  
and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Y is a linkage between a functional group on the transport moiety and a functional  
group on the linker between R<sup>1</sup> and R<sup>3</sup>;

R<sup>3</sup> is the transport moiety;

R<sup>5</sup> is H, OH, SH or NHR<sup>6</sup>;

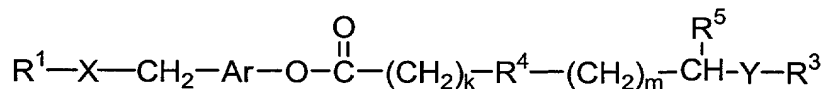
R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

k is 1 or 2.

21. The composition according to claim 20, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate and phosphinate.

22. The composition according to claim 20, wherein each of X and Y is independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and -NHC(O)NH-.

23. The composition according to claim 7, wherein the conjugate has the following structure:



wherein:

R<sup>1</sup> is the biologically active compound;

X is a linkage between a functional group on the biologically active compound  
and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Y is a linkage between a functional group on the transport moiety and a functional  
group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen  
substituents are either *ortho* or *para* to one another;

R<sup>3</sup> is the transport moiety;

R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

R<sup>5</sup> is H, OH, SH, CONHR<sup>6</sup> or NHR<sup>6</sup>;

15 R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;  
16 R<sup>7</sup> and R<sup>8</sup> are independently hydrogen or alkyl; and,  
17 k and m are independently either 1 or 2.

1 24. The composition according to claim 23, wherein each of X and Y is  
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH-, -S-S-,  
3 -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate and  
4 phosphinate.

1 25. The composition according to claim 23, wherein each of X and Y is  
2 independently selected from the group consisting of -C(O)O-, -C(O)NH-, -OC(O)NH- and  
3 -NHC(O)NH-.

1 26. The composition according to claim 12, wherein A is N, R<sup>2</sup> is benzyl,  
2 k, m and n are 1, and X is -C(O)O-.

1 27. The composition according to claim 13, wherein R<sup>4</sup> is S, R<sup>5</sup> is NHR<sup>6</sup>,  
2 R<sup>6</sup> is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1 and X is -C(O)O-.

1 28. The composition according to claim 14, wherein R<sup>5</sup> is NHR<sup>6</sup>, R<sup>6</sup> is  
2 hydrogen, methyl, allyl, butyl or phenyl, k is 2 and X is -C(O)O-.

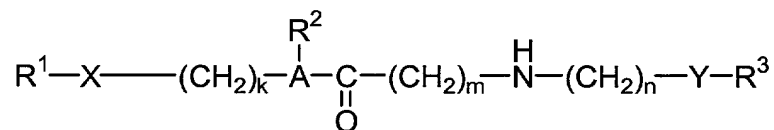
1 29. The composition according to claim 15, wherein Ar is an unsubstituted  
2 aryl group, R<sup>4</sup> is S, R<sup>5</sup> is NHR<sup>6</sup>, R<sup>6</sup> is hydrogen, methyl, allyl, butyl or phenyl, k and m are 1  
3 and X is -C(O)O-.

1 30. A method for increasing the transport of a biologically active  
2 compound across a biological membrane comprising:  
3 administering a composition comprising a biologically active compound and a  
4 transport moiety, wherein the transport compound comprises a structure selected from the  
5 group consisting of (ZYZ)<sub>n</sub>Z, (ZY)<sub>n</sub>Z, (ZYY)<sub>n</sub>Z and (ZYYY)<sub>n</sub>Z, wherein Z is L-arginine or  
6 D-arginine, and wherein Y is an amino acid that does not comprise an amidino or guanidino  
7 moiety, and wherein n is an integer ranging from 2 to 10,  
8 wherein transport of the biologically active compound across the biological  
9 membrane is increased relative to transport of the biologically active compound in the  
10 absence of said transport moiety.

11

1                    31.     The method according to claim 20, wherein the biologically active  
2 compound is attached to the transport moiety by a linking moiety to form a conjugate.

1                    32.     The method of claim 21, wherein the conjugate has the following  
2 structure:



3

4                    wherein:

5                    R<sup>1</sup> is the biologically active compound ;

6                    X is a linkage between a functional group on the biologically active compound  
7                    and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

8                    Y is a linkage between a functional group on the transport moiety and a functional  
9                    group on the linker between R<sup>1</sup> and R<sup>3</sup>;

10                  A is N or CH;

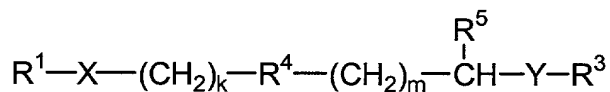
11                  R<sup>2</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

12                  R<sup>3</sup> is a transport moiety;

13                  k and m are independently either 1 or 2; and

14                  n is an integer of from 1 to 10.

1                    33.     The method of claim 21, wherein the conjugate has the following  
2 structure:



3

4                    wherein:

5                    R<sup>1</sup> is the biologically active compound ;

6                    X is a linkage between a functional group on the biologically active compound  
7                    and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

8                    Y is a linkage between a functional group on the transport moiety and a functional  
9                    group on the linker between R<sup>1</sup> and R<sup>3</sup>;

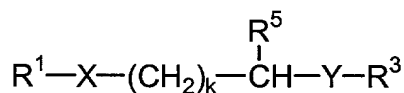
10                  R<sup>3</sup> is a transport moiety;

11                  R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

12                  R<sup>5</sup> is OH, SH or NHR<sup>6</sup>;

R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;  
 R<sup>7</sup> and R<sup>8</sup> are independently hydrogen, alkyl or arylalkyl; and  
 k and m are independently either 1 or 2.

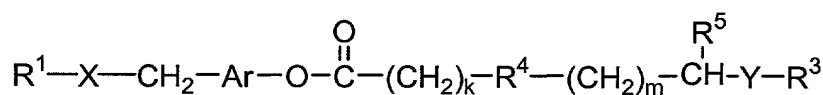
34. The method of claim 21, wherein the conjugate has the following structure:



wherein:

R<sup>1</sup> is the biologically active compound;  
 X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;  
 Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;  
 R<sup>3</sup> is the transport moiety;  
 R<sup>5</sup> is H, OH, SH or NHR<sup>6</sup>;  
 R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and  
 k is 1 or 2.

35. The method of claim 21, wherein the conjugate is of the following structure:



wherein:

R<sup>1</sup> is the biologically active compound;  
 X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;  
 Y is a linkage between a functional group on the transport moiety and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;  
 Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;  
 R<sup>3</sup> is the transport moiety;  
 R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;  
 R<sup>5</sup> is H, OH, SH, CONHR<sup>6</sup> or NHR<sup>6</sup>;

- 15  $R^6$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;  
16  $R^7$  and  $R^8$  are independently hydrogen or alkyl; and,  
17 k and m are independently either 1 or 2.

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